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10/568,433	08/08/2006	Gilles Pain	010180.00049	9995
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BANNER & WITCOFF, LTD. 1100 13th STREET, N.W. SUITE 1200 WASHINGTON, DC 20005-4051			JARRELL, NOBLE E	
ART UNIT	PAPER NUMBER		1624	
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/568,433	<b>Applicant(s)</b> PAIN ET AL.
	<b>Examiner</b> NOBLE JARRELL	<b>Art Unit</b> 1624

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If no period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### **Status**

1) Responsive to communication(s) filed on 03 August 2009.  
 2a) This action is FINAL.      2b) This action is non-final.  
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### **Disposition of Claims**

4) Claim(s) 1-4,6,8-11,14-22,24 and 26 is/are pending in the application.  
 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.  
 5) Claim(s) \_\_\_\_\_ is/are allowed.  
 6) Claim(s) 1-4,6,8-11,15,16,20-22,24 and 26 is/are rejected.  
 7) Claim(s) 14 and 17-19 is/are objected to.  
 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### **Application Papers**

9) The specification is objected to by the Examiner.  
 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### **Priority under 35 U.S.C. § 119**

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
 a) All    b) Some \* c) None of:  
 1. Certified copies of the priority documents have been received.  
 2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### **Attachment(s)**

1) Notice of References Cited (PTO-892)  
 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)  
 3) Information Disclosure Statement(s) (PTO/SB/08)  
 Paper No(s)/Mail Date \_\_\_\_\_

4) Interview Summary (PTO-413)  
 Paper No(s)/Mail Date. \_\_\_\_\_

5) Notice of Informal Patent Application  
 6) Other: \_\_\_\_\_

## **DETAILED ACTION**

### **Response to Amendment**

1. The rejections under 35 U.S.C. 112 1<sup>st</sup> and 2<sup>nd</sup> paragraph have been overcome by the amendment filed 8/3/2009.
2. In the current set of claims, claims 1-4, 6, 8-11, 14-22, 24, and 26 are pending (and consequently being examined on the merits).

### ***Claim Rejections - 35 USC § 102***

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351 (a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

4. Claims 1, 2, 6, 8, 9, 10, 11, 15, 16, 20, 22, 24, and 26 are rejected under 35 U.S.C. 102(e) as being anticipated by Swinnen et al. (US20080021028, published 24 January 2008, filed 25 July 2005, claims priority to 60/591111, filed 26 July 2004). Swinnen et al. teach the following compounds that anticipate compounds of instant formula (I) embraced by the specified claims of application 10/568433: example 6 (paragraph 0712, page 42), example 7 (paragraph 0716, page 43), example 8 (paragraph 0720, page 43), example 9 (paragraph 0724, page 44), example 19 (paragraph 0766, page 49), example 21 (paragraph 0733, page 50), example 23 (paragraph 0772, page 51), example 24 (paragraph 0779, page 51), example 25 (paragraph 0781, page 51), example 26 (paragraph 0783, page 51), example 27 (paragraph 0785, page 52), example 30 (paragraph 0791, page 52), example 31 (paragraph 0793, page 53), example 32 (paragraph 0795, page 53), example 33 (paragraph 0797, page 53), example 34 (paragraph 0799, page 53), example 35 (paragraph 0801, page 54), example 36 (paragraph 0803, page 54), example 37

(paragraph 0805, page 54), example 38 (paragraph 0807, page 54), example 39 (paragraph 0809, page 55), example 40 (paragraph 0811, page 55), example 41 (paragraph 0813, page 55), example 64 (paragraph 0863, page 61), example 65 (paragraph 0867, page 62), example 76 (paragraph 0889, page 64), and example 77 (paragraph 0891, page 64).

In the specified examples, variable R of application 10/568433 is a hydrogen atom. In claim 1 of application 10/568433, variable R is selected from hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl, or C<sub>3</sub>-C<sub>6</sub> cycloalkyl.

The groups that represent chemical moiety (Alk)-Ar of formula (I) of application 10/568433 in the examples of Swinnen et al. are the following: propylene-4-ethoxy-phenylene, propylene-4-(O-CF<sub>3</sub>)-phenylene, and CH<sub>2</sub>-phenyl (benzyl). In application 10/568433, variable "Alk" can represent a divalent C<sub>1</sub>-C<sub>5</sub> alkylene radical and variable "Ar" is an optionally substituted phenyl ring. The phenyl ring of variable "Ar" can be substituted with a (C<sub>1</sub>-C<sub>3</sub>)alkoxy or trifluoromethoxy group among other possibilities.

The groups that represent moiety NR<sub>1</sub>R<sub>2</sub> of application 10/568433 in Swinnen et al. are the following: 4-(2-pyridinyl)-2-methyl-piperazin-1-yl, 4-(2-pyrimidinyl)-2-methyl-piperazin-1-yl, 4-(2-fluorophenyl)-2-methyl-piperazin-1-yl, 4-(4-fluorophenyl)-piperazin-1-yl, 4-[5-trifluoromethyl-2-pyridinyl]-piperazin-1-yl, 4-[5-cyano-2-pyridinyl]-piperazin-1-yl, 4-[6-methyl-2-pyridinyl]-piperazin-1-yl, 4-[6-chloro-2-pyridinyl]-piperazin-1-yl, 5-[6-chloro-2-pyridinyl]-piperazin-1-yl, 4-[4-chloro-2-fluorophenyl]-piperazin-1-yl, 4-[2-chlorophenyl]-piperazin-1-yl, 4-[6-methyl-2-(trifluoromethyl)-4-quinolinyl]-piperazin-1-yl, 4-[3-(trifluoromethyl)-2-pyridinyl]-piperazin-1-yl, 4-[2-pyrazinyl]-piperazin-1-yl, 4-[2-(4-morpholinyl)ethyl]-piperazin-1-yl, 4-[2-cyanophenyl]-piperazin-1-yl, 4-[2-pyridinyl]-piperazin-1-yl, 4-[2-(2-thienyl)ethyl]-piperazin-1-yl, 4-cyclohexyl-piperazin-1-yl, 4-[4-(trifluoromethoxy)phenyl]-piperazin-1-yl, and 4-[4-(trifluoromethoxy)phenyl]-2-methyl-piperazin-1-yl. In application 10/568433, variables R<sub>1</sub> and R<sub>2</sub> taken together with the nitrogen to which they are attached form a piperazine ring. This piperazine ring is substituted with at least one instance of formula (II). Variable Z of formula (II) can be an

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optionally substituted carbocyclic or heterocyclic group. In the compounds taught by Swinnen et al., variable Z is a pyridine ring with or without substituents, an unsubstituted pyrimidine ring, a substituted phenyl ring, an ethylene-2-thienyl (in variable Z, one of variable "Alk<sup>1</sup>" or "Alk<sup>2</sup>" is ethylene (variable m or n is one) or each one of variables "Alk<sup>1</sup>" and "Alk<sup>2</sup>" is a methylene group (variables m and n are each one)), and cyclohexyl.

Compositions comprising these compounds are taught on pages 22 to 23 (paragraphs 0544 to 0551). These compounds can be used in the treatment of arthritis (page 22, paragraph 0542, line 6). It is noted that these compounds are useful in other disorders (page 22, paragraphs 0539 to 0542).

#### ***Claim Rejections - 35 USC § 103***

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

7. Claims 1, 3, 4, 6, 8, 9, 10, 11, 15, 16, 20, 21, 22, 24, and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Swinnen et al. (US20080021028, published 24 January 2008, filed 25 July 2005, claims priority to 60/591111, filed 26 July 2004) in view of Wermuth (*The Practice of Medicinal Chemistry*, 1996, pages 203-37).

#### ***Determining the scope and contents of the prior art***

Swinnen et al. teach the following compounds: example 6 (paragraph 0712, page 42), example 7 (paragraph 0716, page 43), example 8 (paragraph 0720, page 43), example 9 (paragraph 0724, page 44), example 19 (paragraph 0766, page 49), example 21 (paragraph 0733, page 50), example 23 (paragraph 0772, page 51), example 24 (paragraph 0779, page 51), example 25 (paragraph 0781, page 51), example 26 (paragraph 0783, page 51), example 27 (paragraph 0785, page 52), example 30 (paragraph 0791, page 52), example 31 (paragraph 0793, page 53), example 32 (paragraph 0795, page 53), example 33 (paragraph 0797, page 53), example 34 (paragraph 0799, page 53), example 35 (paragraph 0801, page 54), example 36 (paragraph 0803, page 54), example 37 (paragraph 0805, page 54), example 38 (paragraph 0807, page 54), example 39 (paragraph 0809, page 55), example 40 (paragraph 0811, page 55), example 41 (paragraph 0813, page 55), example 64 (paragraph 0863, page 61), example 65 (paragraph 0867, page 62), example 76 (paragraph 0889, page 64), and example 77 (paragraph 0891, page 64).

In the specified examples, variable R of application 10/568433 is a hydrogen atom. In claim 1 of application 10/568433, variable R is selected from hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl, or C<sub>3</sub>-C<sub>6</sub> cycloalkyl..

The groups that represent chemical moiety (Alk)-Ar of formula (I) of application 10/568433 in the examples of Swinnen et al. are the following: propylene-4-ethoxy-phenylene, propylene-4-(O-CF<sub>3</sub>)-phenylene, and CH<sub>2</sub>-phenyl (benzyl). In application 10/568433, variable "Alk" can represent a divalent C<sub>1</sub>-C<sub>5</sub> alkylene radical and variable "Ar" is an optionally substituted phenyl ring. The phenyl ring of variable "Ar" can be substituted with a (C<sub>1</sub>-C<sub>3</sub>)alkoxy or trifluoromethoxy group among other possibilities.

The groups that represent moiety NR<sub>1</sub>R<sub>2</sub> of application 10/568433 in Swinnen et al. are the following: 4-(2-pyridinyl)-2-methyl-piperazin-1-yl, 4-(2-pyrimidinyl)-2-methyl-piperazin-1-yl, 4-(2-fluorophenyl)-2-methyl-piperazin-1-yl, 4-(4-fluorophenyl)-piperazin-1-yl, 4-[5-trifluoromethyl-2-pyridinyl]-piperazin-1-yl, 4-[5-cyano-2-pyridinyl]-piperazin-1-yl, 4-[6-methyl-2-pyridinyl]-piperazin-1-yl, 4-

[6-chloro-2-pyridinyl]-piperazin-1-yl, 5-[6-chloro-2-pyridinyl]-piperazin-1-yl, 4-[4-chloro-2-fluorophenyl]-piperazin-1-yl, 4-[2-chlorophenyl]-piperazin-1-yl, 4-[6-methyl-2-(trifluoromethyl)-4-quinoliny]-piperazin-1-yl, 4-[3-(trifluoromethyl)-2-pyridinyl]-piperazin-1-yl, 4-[2-pyrazinyl]-piperazin-1-yl, 4-[2-(4-morpholinyl)ethyl]-piperazin-1-yl, 4-[2-cyanophenyl]-piperazin-1-yl, 4-[2-pyridinyl]-piperazin-1-yl, 4-[2-(2-thienyl)ethyl]-piperazin-1-yl, 4-cyclohexyl-piperazin-1-yl, 4-[4-(trifluoromethoxy)phenyl]-piperazin-1-yl, and 4-[4-(trifluoromethoxy)phenyl]-2-methyl-piperazin-1-yl. In application 10/568433, variables R<sub>1</sub> and R<sub>2</sub> taken together with the nitrogen to which they are attached form a piperazine ring. This piperazine ring is substituted with at least one instance of formula (II). Variable Z of formula (II) can be an optionally substituted carbocyclic or heterocyclic group. In the compounds taught by Swinnen et al., variable Z is a pyridine ring with or without substituents, an unsubstituted pyrimidine ring, a substituted phenyl ring, an ethylene-2-thienyl (in variable Z, one of variable "Alk<sup>1</sup>" or "Alk<sup>2</sup>" is ethylene (variable m or n is one) or each one of variables "Alk<sup>1</sup>" and "Alk<sup>2</sup>" is a methylene group (variables m and n are each one)), and cyclohexyl.

Swinnen et al. teach that variable R<sup>3</sup> (this variable is attached to the carbon α to C(O)NHOH group in the examples) in US 2008021028 can be a hydrogen atom, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>2</sub>-C<sub>6</sub> alkenyl, or C<sub>2</sub>-C<sub>6</sub> alkynyl (see claim 1). Thus, Swinnen et al. teach equivalency between a hydrogen atom and an alkyl group for these types of compounds.

Compositions comprising these compounds are taught on pages 22 to 23 (paragraphs 0544 to 0551). These compounds can be used in the treatment of arthritis (page 22, paragraph 0542, line 6). It is noted that these compounds are useful in other disorders (page 22, paragraphs 0539 to 0542).

Wermuth (section IV, pages 226-228) teaches a chloro group is commonly substituted for a hydrogen or fluorine group on a phenyl ring (pages 226-228). Wermuth also teaches that halogens can replace hydrogen in medicinal chemistry (section (d), page 228).

***Ascertaining the differences between the prior art and the claims at issue***

In the prior art (Swinnen et al.), variable R of application 10/568433 is a hydrogen atom.

Swinnen et al. also teach that variable R<sup>3</sup> (the equivalent of variable R in application 10/568433) in US 2008021028 can be a hydrogen atom, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>2</sub>-C<sub>6</sub> alkenyl, or C<sub>2</sub>-C<sub>6</sub> alkynyl (see claim 1). Thus, Swinnen et al. teach equivalency between a hydrogen atom and an alkyl group for these types of compounds. Swinnen et al. also teach equivalency between hydrogen and alkyl substituents when attached to piperazine ring (see variables R<sup>4</sup> and R<sup>6</sup>, page 7, column 2, lines 9-14). Several of the compounds taught by Swinnen et al. have the (S, S) stereochemical designation and others have a (R, S) stereochemical designation. In other words, several of the compounds taught by Swinnen et al. are diastereomers of compounds claimed in the instant application.

In claims 1, 3, 4, 6, 8, 9, 10, 11, 15, 16, 20, 21, 22, 24, and 26 of application 10/568433, variable R is methyl, ethyl, n-propyl, isopropyl, n-butyl, s-butyl, or t-butyl. In claim 21, the stereochemical designation of each compound is (R, S).

***Resolving the level of ordinary skill in the pertinent art***

Those of relative skill in the art are those with level of skill of the authors of the references cited to support the examiner's position. The relative skill of those in this art is MD's, PhD's, or those with advanced degrees and the requisite experience in preparation of compounds of the elected group.

***Considering objective evidence present in the application indicating obviousness or nonobviousness***

*In re Norris* (84 USPQ 458) teaches "Counsel for applicant in their brief acknowledge that the record herein does not establish new and useful compound defined by the rejected claim possesses one or more specifically identified properties to be recognized as unobvious or unexpected, as measured by every conceivable standard. Since the product claimed herein admittedly possesses no unexpected characteristics or properties, in view of what has hereinbefore been said, it is not patentable."

*In re Lohr and Spurlin* (137 USPQ 548) teaches: When a new compound so closely related to a prior art compound as to be structurally obvious is sought to be patented based on the alleged greater effectiveness of the new compound for the same purpose as the old compound, clear and convincing evidence of substantially greater effectiveness is needed. Here there are no new properties, but merely an alleged improvement in the same property for use against the same pests.

Compounds 1, 2, 3, 4, 8, 13, 28, 29, and 43 of claim 22 are rendered obvious by specific compounds of Swinnen (the exact relationships are shown in the table below).

<u>Compound # of claim 21 of application</u>	<u>Examples taught by Swinnen et al.</u>
<u>10/568433</u>	
1, 2	34
3, 4, 29	6 and 7
8	8
13, 28	9, 19, 27, and 30
43	9, 19, and 39

Example 34 renders compounds 1 and 2 of claim 21 because this compound is a positional isomer of these two compounds. In compounds 1 and 2, the methoxy group is attached to the 3 or 4-position of the phenyl ring. In example 34, the methoxy group is attached to 2-position of the phenyl ring. Sufficient motivation to prepare this compound exists because this compound is being used in an identical method to what is claimed in claims 24 and 26 of application 10/568433.

Examples 6 and 7 of Swinnen et al. render compounds 3, 4, and 29 of claim 21 obvious because the differences between these sets of compounds are the stereochemical designations, the position of the fluoro group on the phenyl ring, the presence of a chloro substituent instead of hydrogen substituent at the *para* position, and the presence of a chloro group at the *ortho* position of the phenyl ring. Specifically, examples 6 and 7 are each the (S, S) diastereomers of compounds 3, 4, and 28. In a

comparison of compounds 3 and 4 with examples 6 and 7, the point of attachment to the pyridine ring is different (in compounds 3 and 4, the point of attachment is *para*; in examples 6 and 7, the point of attachment is *ortho*). Compound 29 is obvious because variable Ar is substituted with a methoxy group. *In re Lohr and Spurlin* teaches that when a compound is different by an alkyl group (in a comparison of Swinnen et al. and compound 29 of claim 21 of 10/568433, the difference is CH<sub>2</sub> between methoxy and ethoxy), clear and convincing evidence of substantially greater effectiveness is needed. As stated previously, sufficient motivation to prepare and use these compounds exists, because Swinnen et al. are using examples 6 and 7 for the same purpose as the instant application (treatment of arthritis).

Example 8 of Swinnen et al. renders compound 8 of claim 21 obvious due to positional isomerism. The other difference between these compounds is the stereochemistry of the asymmetric centers (example 8 is (S, S) and compound 8 is (R, S)). In example 8, the point of attachment to the pyrimidine ring is at the 2-position. In compound 8 of claim 21, the point of attachment to the pyrimidine ring is the 4-position. Sufficient motivation to prepare and use these compounds exists, because Swinnen et al. are using examples 6 and 7 for the same purpose as the instant application (treatment of arthritis). Even though the stereochemical designation between the two compounds and the point of attachment to the pyrimidine ring is different, reasonable expectation of success exists (due to the same method of use).

Examples 9, 19, 27, 30 of Swinnen et al. render obvious compounds 13 and 28 of claim 21 obvious because of several reasons. Example 9 differs from compounds 13 and 28 because of the stereochemical designation of compound 13, (S, S), the presence of an ethoxy group instead of a methoxy group (compound 28), and methyl group attached to the 2-position of the piperazine ring. Swinnen et al. teach that an alkyl group is equivalent to a hydrogen atom in compounds of formula I (page 7, column, lines 9-14). More specifically, variables R<sup>4</sup> and R<sup>6</sup> can be hydrogen or an alkyl group. Example 19 is a positional isomer of compound 13 (example 19 is *p*-F-phenyl and compound 13 is *o*-F-

phenyl). In example 19 of Swinnen et al., two differences between this example and compound 28 exist: NR<sub>1</sub>R<sub>2</sub> is 4-[4-fluorophenyl]-piperazin-1-yl and 4-ethoxyphenyl for variable Ar. Example 27 differs from compound 13 due to the presence of a *p*-Cl-*o*-F-phenyl group instead of a *p*-F-phenyl group. In light of Wermuth, example 27 is an obvious variant of compound 13 because a chloro group can take the place of a hydrogen group in medicinal chemistry. Example 27 of Swinnen et al. is different from compound 28 of application 10/568433 in the following aspects: NR<sub>1</sub>R<sub>2</sub> is 4-[4-chloro-2-fluorophenyl]-piperazin-1-yl and variable Ar is 4-ethoxyphenyl. In an application of Wermuth and *In re Lohr and Spurlin* to example 27 of Swinnen et al., this example renders compound 28 of claim 22 obvious. An ethoxy group differs from a methoxy group by a methylene group (hence an ethoxy group is analogous to a methoxy group) and substitution of chloro for hydrogen is known in medicinal chemistry. Example 30 is a positional isomer of compound 13 because variable Ar is *o*-Cl-phenyl in example 30 and *o*-F-phenyl in compound 13. Chlorine is part of the same periodic family as fluorine (the halogens). Swinnen et al. show that their compounds are used for the same purpose as the instant application. In addition, Wermuth teaches that substitution of a fluoro group with a chloro group is known in medicinal chemistry. Example 30 is different from compound 28 in the following aspects: NR<sub>1</sub>R<sub>2</sub> is 4-[2-chlorophenyl]-piperazin-1-yl and variable Ar is 4-ethoxyphenyl. It has already been noted that the cited examples of Swinnen are being used for the same purpose as the instant application (the treatment of arthritis). Because compounds of Swinnen et al. are being used in an identical purpose to application, a reasonable expectation of success exists. The position of the fluoro group when group NR<sub>1</sub>R<sub>2</sub> is 4-[2 (or 4)-fluorophenyl]-piperazin-1-yl is not critical because Swinnen et al. teach compounds with fluoro at both positions.

Examples 9, 19, 30, and 35 render compound 43 of claim 22 obvious. In example, NR<sub>1</sub>R<sub>2</sub> is 4-[2-fluorophenyl]-2-methyl-piperazin-1-yl, variable Ar is 4-ethoxyphenyl, and variable R is H. In example 19, NR<sub>1</sub>R<sub>2</sub> is 4-[4-fluorophenyl]-piperazin-1-yl, variable Ar is 4-ethoxyphenyl, and variable R is H. In

example 30, NR<sub>1</sub>R<sub>2</sub> is 4-[2-chlorophenyl]-piperazin-1-yl, variable Ar is 4-ethoxyphenyl, and variable R is H. In example 35, NR<sub>1</sub>R<sub>2</sub> is 4-[4-chlorophenyl]-piperazin-1-yl, variable Ar is 4-ethoxyphenyl, and variable R is H. In compound 43 of claim 21, variable R is methyl, Ar is 4-ethoxyphenyl, and NR<sub>1</sub>R<sub>2</sub> is 4-[2-fluorophenyl]-piperazin-1-yl. Swinnen et al. teach that an OH group is equivalent to an O-alkyl group when the OH or O-alkyl group is attached to the carbon  $\alpha$  to the C(O)NH(OH) group of the compound. In claim 1 of Swinnen, both hydrogen and alkyl are listed as possibilities for variable R<sup>3</sup> (which is equivalent to variable R of application 10/568433). As stated previously, the compounds of Swinnen et al. are being used for the same purpose as the instant application. Consequently, sufficient motivation exists to prepare the compounds of Swinnen et al.

#### **Conclusion**

8. Claims 14, 17, 18, and 19 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

9. The following is a statement of reasons for the indication of allowable subject matter: Claims 14 and 17 appear free of the prior art of record because Swinnen et al. do not teach compounds in which variable Z of formula (II) is hydrogen and/or variable p of group (II) is one. Claims 18 and 19 appear free of the prior art of record because Swinnen et al. do not teach compounds in which the group NR<sub>1</sub>R<sub>2</sub> is 4-(SO<sub>2</sub>R<sub>5</sub> or COR<sub>5</sub>)-piperazin-1-yl wherein variable R<sub>5</sub> is an alkyl or cyclic group. Swinnen et al. (same reference as cited above) teach compounds in which NR<sub>1</sub>R<sub>2</sub> is 4-(hetero)aryl-piperazin-1-yl.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NOBLE JARRELL whose telephone number is (571)272-9077. The examiner can normally be reached on M-F 7:30 A.M - 6:00 P.M. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson can be reached on (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Noble Jarrell/  
Examiner, Art Unit 1624

/James O. Wilson/  
**Supervisory Patent Examiner, Art Unit 1624**